CLAIMS

1. A method for preparing daptomycin, comprising the steps of providing an amorphous form of daptomycin and crystallizing the daptomycin from a crystallization solution comprising a cation from a salt, a buffer, an organic precipitant, and a low molecular weight alcohol.

2. The method according to claim 1, wherein the buffer is selected from the group consisting of HEPES, Tris HCl, imidazole, MES, CHES, a citrate salt and a cacodylate salt.

3. The method according to claim 1, wherein the alcohol is selected from the group consisting of ethylene glycol, propylene glycol, t-butanol, glycerol, isopropanol, 1,4-butanediol, 1,2-propanediol and methanol.

4. The method according to claim 1, wherein the organic precipitant is polyethylene glycol or polyethylene glycol monomethyl ether.

5. The method according to claim 1, wherein the crystallizing solution further comprises a divalent cation.

6. The method according to claim 5, wherein the divalent cation is calcium, zinc or magnesium.

7. The method according to claim 1, wherein the pH of the crystallization solution is in the range of 5 to 8.5.

8. The method according to claim 7, wherein the pH of the crystallization solution is in the range of 5.5 to 7.5.

9. The method according to claim 8, wherein the pH of the crystallization solution is in the range of 5.9 to 6.6.

10. The method according to claim 1, wherein the crystallization is done by the hanging drop method or by batch crystallization.

11. The method according to claim 1, wherein a crystal of the daptomycin is an urchin-like or a cluster of needles form.

12. The method according to claim 1, wherein a crystal of the daptomycin is a rod-like form.

13. The method according to claim 1, further comprising the step of collecting the daptomycin crystals.

14. The method according to claim 13, wherein said collecting is done by centrifugation, precipitation or filtration.

15. The method according to either of claims 1 or 14, further comprising washing the crystalline daptomycin.

16. The method according to claim 1, wherein the daptomycin is at a starting purity of at least 90%.

17. The method according to claim 1, wherein the daptomycin is at a starting purity of at least 93%.

18. The method according to claim 1, wherein said crystallizing is performed at a temperature below 20°C.

19. The method according to claim 18, wherein said crystallizing is performed at about 4°C.

20. The method according to claim 1, wherein said crystallizing is performed at above 20°C.

21. The method according to claim 1, wherein said crystallizing is performed with stirring.

22. A method for preparing a crystalline or crystal-like daptomycin, comprising the steps of

a) providing a solution comprising daptomycin, a salt comprising a monovalent or divalent cation, a pH buffering agent and a low molecular weight or polyhydric alcohol; and

b) allowing the daptomycin to crystallize or precipitate from the solution to obtain a crystalline or crystal-like daptomycin preparation, respectively.

23. The method according to claim 22, wherein the buffering agent is selected from the group consisting of HEPES, Tris HCl, imidazole, MES, CHES, sodium acetate, calcium acetate, a citrate salt and a cacodylate salt.

24. The method according to claim 22, wherein the alcohol is selected from the group consisting of ethylene glycol, propylene glycol, t-butanol, glycerol, isopropanol, 1,4-butanediol, 1,2-propanediol and methanol.

25. The method according to claim 24, wherein the alcohol is isopropanol.

26. The method according to claim 22, wherein the salt comprises a divalent cation.

27. The method according to claim 26, wherein the divalent cation is a magnesium cation, a zinc cation or a calcium cation.

28. The method according to claim 27, wherein the divalent cation is a calcium cation.

29. A method for preparing a crystalline or crystal-like daptomycin, comprising the steps of

a) providing a solution comprising daptomycin, a pH buffering agent that is a salt comprising a monovalent or divalent cation, and a low molecular weight or polyhydric alcohol; and

b) allowing the daptomycin to crystallize or precipitate from the solution to obtain a crystalline or crystal-like daptomycin preparation, respectively.

30. The method according to claim 29, wherein the buffering agent comprises a divalent cation selected from a calcium cation or a magnesium cation.

31. The method according to claim 22 or claim 29, wherein the pH of the solution is in the range of 5.0 to 9.5.

32. The method according to claim 31, wherein the pH of the solution is in the range of 5.5 to 7.5.

33. The method according to claim 32, wherein the pH of the solution is in the range of 5.9 to 6.3.

34. The method according to either of claims 22 or 29, wherein said crystallizing or precipitating step is done at a temperature of 0-30°C.

35. The method according to claim 34, wherein the temperature is 23-28°C.

36. The method according to claim 29, wherein the solution comprises calcium acetate pH 6.1 and isopropanol.

37. The method according to claim 36, wherein said crystallizing or precipitating step comprises adding isopropanol until the mixture becomes cloudy.

38. The method according to claim 37, wherein said crystallizing or precipitating step is done for a period of time of from one hour to three weeks.

39. The method according to claim 22, wherein said crystallizing or precipitating is done by batch crystallization or batch precipitation, respectively.

40. The method according to claim 22 or claim 29, further comprising the step of collecting the crystalline or crystal-like daptomycin.

41. The method according to claim 40, wherein said collecting step is performed by filtration or centrifugation.

42. The method according to claim 41, wherein said collecting is performed by filtration.

43. The method according to claim 40, further comprising the step of washing the crystalline or crystal-like daptomycin.

44. The method according to claim 22 or claim 29, wherein the crystalline or crystal-like daptomycin has an urchin-like form.

45. The method according to claim 22 or 29, wherein the daptomycin has a purity before crystallizing or precipitating of no greater than 90% and has a purity after crystallization or precipitation of at least 95%.

46. The method according to claim 45, wherein the daptomycin has a purity before crystallizing or precipitating of no greater than 80% and has a purity after crystallization or precipitation of at least 95%.

47. The method according to claim 45, wherein the daptomycin has a purity before crystallizing or precipitating of no greater than 60% and has a purity after crystallization or precipitation of at least 95%.

48. The method according to claim 45, wherein the daptomycin has a purity before crystallizing or precipitating of no greater than 40% and has a purity after crystallization or precipitation of at least 95%.

49. The method according to claim 45, wherein the daptomycin is at a starting purity of no greater than 10% and has a purity after crystallization or precipitation of at least 95%.

50. The method according to any one of claims 46-50, wherein the daptomycin has a purity after crystallization or precipitation of at least 96%.

51. The method according to any one of claims 46-50, wherein the daptomycin has a purity after crystallization or precipitation of at least 97%.

52. The method according to any one of claims 46-50, wherein the daptomycin has a purity after crystallization or precipitation of at least 98%.

53. A method for preparing a purified daptomycin, comprising the steps of

a) providing a solution comprising daptomycin, a pH buffering agent that is a salt comprising a monovalent or divalent cation, and a low molecular weight or polyhydric alcohol; and

b) allowing the daptomycin to crystallize or precipitate from the solution to obtain a purified daptomycin preparation.

54. The method according to claim 53, wherein the purified daptomycin preparation is at least 95% pure.

55. The method according to claim 54, wherein said purified daptomycin preparation is at least 96% pure.

56. The method according to claim 55, wherein said purified daptomycin preparation is at least 97% pure.

57. The method according to claim 56, wherein said purified daptomycin preparation is at least 98% pure.